

Subscribing to Bandolier

On page 8 of April's **Bandolier** you will find a subscription form for those of you who wish to continue to receive a monthly copy when NHS funding ceases after July. By filling in the form and returning it to us, your **Bandolier** will continue. Health service organisations and charities who can take **Bandolier** in bulk and distribute it themselves, or those who would like a bulk order for us to distribute, can contact us for preferential rates. The aim will always be to keep costs to the public sector to a minimum.

No **Bandolier** after July unless you take out a subscription.

Electronic update

In the last few months **Bandolier** has been busy increasing the amount of material available on the Internet. Three areas have been extended.

We have been collecting systematic reviews in the area of benign prostatic hyperplasia, and the new BPH centre has a range of reviews on conventional and unconventional therapies.

Multiple sclerosis has been in the news of late, and what evidence we could find has been collected. This includes two new reviews. One is on intravenous immunoglobulins available on-screen and as a downloadable PDF. The second involves the use of cannabis for spasticity, including spasticity related to MS. There is evidence but little of quality, though there is some scientific background emerging. It is impossible to do a formal review, but what evidence that can be found is being collected and abstracted on-screen.

The **Bandolier** migraine site has also undergone a refit, with a number of important interventions updated and with results on different outcomes added. Also available is a special issue of **Bandolier Extra** on migraine as a downloadable PDF.

EDITORS

Andrew Moore Henry McQuay
Pain Relief Unit
The Churchill, Oxford OX3 7LJ
Editorial office: 01865 226132
Editorial fax: 01865 226978
Email: bandolier@pru.ox.ac.uk
Internet: www.ebandolier.com
ISSN 1353-9906

COPD AND TREATMENT

Bandolier thought the diagnostic algorithm for chronic obstructive pulmonary disease (COPD, or chronic obstructive airways disease COAD) determined through the CARE process was wonderful (**Bandolier** 78), though the limitations of treatment sobering. Smoking more than 40 pack-years was the biggest predictor for COPD. A fifth of long-term smokers have a reduced forced expiratory volume over one second (FEV1), defined as more than two standard deviations below that for a normal population of that age. There follows increasing dyspnoea and other respiratory symptoms, with progressive deterioration of health status.

Background

In nonsmokers the FEV1 falls with age, so that by 75 years it may be 75% or so of the value obtained at 25 years, but in some smokers it can fall dramatically faster. Stopping smoking reduces the speed of decline. Otherwise treatments are palliative, with inhaled anticholinergic drugs as the mainstay. Two recent publications of the same review are authoritative regarding the evidence available on the treatment of acute exacerbations [1,2], including diagnostic tests and prognostic factors.

About 5-15% of adults in industrialized countries have COPD defined by spirometry. In 1990, COPD was the twelfth most common cause of combined mortality and disability but is expected to become the fifth cause by the year 2020. After diagnosis the 10-year survival rate is approximately 50% with more than one-third of patients dying due to respiratory insufficiency.

There are about 16 million patients with COPD in the USA, and the prevalence in adults between 40 and 70 years is about 10%. A UK primary care organisation of 100,000 would have, on average, about 40,000 people over 40 years, with about 4,000 patients with COPD on their books. In a proportion it would be moderate or severe.

In this issue

COPD	p. 1
Stents and thrombosis	p. 4
CABG mortality	p. 5
Do formularies work?	p. 7
Getting Bandolier after July	p. 8

*The views expressed in **Bandolier** are those of the authors, and are not necessarily those of the NHSE*

The problems when COPD is moderate or severe are several fold. First is a reduced health status, inability to work, and increasing dependence. Then there are the exacerbations of breathlessness and sputum production. Finally, of course there is hospital admission.

Exacerbation and hospital admission

A large cross-sectional observational study on ambulatory COPD patients in primary care sought to find predictors of exacerbations and hospital admission in 201 general practices in Spain. It used sensible definitions for diagnosis, and exacerbation. Information was collected on 1,001 patients, and was detailed, and included spirometry. Randomly selected patients were used to test and validate models for predicting exacerbation and hospital admission.

Two or more exacerbations a year were suffered by 55%, and 22% had a hospital admission. Two or more exacerbations occurred more often in older patients, those with chronic mucus hypersecretion and those with more severe FEV1 impairment. At least one hospital admission occurred more frequently in older patients, those with more comorbid illnesses and with more severe FEV1 impairment.

There are limits to the utility of this information except that it hints at the sorts of patients more likely to be in trouble, and probably does no more than confirm clinical feel in primary care. It also shows the importance of the surrogate measure of FEV1. In other studies, like one looking at five-year survival after discharge with first admission with COPD [4], the crude five-year mortality rate was 45%. It increased with older age and lower FEV1.

Tiotropium

A new potential treatment heaves into view with publication of two randomised trials [5,6] from each side of the Atlantic (the way the FDA demands) plus a thoughtful edi-

torial [7]. The interesting thing is that these studies were large and had a one-year duration, enough to investigate the effect on exacerbations and hospital admission.

Trials

These had similar designs, being randomised and double blind, patients having a smoking history of 10 pack years or more, an FEV1 of 65% or less of predicted for age, and were at least 40 years of age. Asthma, allergic rhinitis, atopy or elevated eosinophil counts were exclusions, as were patients needing regular supplementary oxygen, recent respiratory tract infection, or with significant comorbid conditions. They received tiotropium 18 µg each morning, or placebo (USA) or ipratropium 40 µg four times a day. The duration of the studies was one year.

Results

Patients were well matched at baseline in each trial, were mostly male, and had an average age of about 65 years. There were a number of outcomes. The main results (all with statistical significance between tiotropium and control for efficacy measures) are shown in Table 1.

Tiotropium improved FEV1 (measured before dosing at the end of the year) and the proportion of patients with clinically significant improvement in symptom scores. In the European study a clinically meaningful improvement of four units in the St George's Respiratory Questionnaire was found in 52% of patients on tiotropium and 35% of those on ipratropium (an NNT of about 6).

Exacerbations were reduced with tiotropium, as were hospital admissions. Combining the two studies because the results with placebo and ipratropium for these outcomes were about the same, we can calculate NNTs. For exacerbations, 323/906 (36%) of patients treated with tiotropium had at least one exacerbation, compared with

Table 1: Main results in two randomised trials of tiotropium in the USA and in Europe

	US Study		European study	
	Tiotropium	Placebo	Tiatropium	Ipratropium
Quality score (out of 5)	4		4	
Number of patients	550	371	356	179
Spirometry				
Baseline FEV1 (L/one second)	1.04	1.00	1.25	1.18
Change in FEV1 (before dose, L)	+0.12	-0.03	+0.12	-0.03
Symptoms				
Clinically important symptoms improvement (% in five assessments)	42-47	29-34	31	18
Exacerbations				
At least one exacerbation (%)	36	42	35	46
Exacerbations per patient per year	0.76	0.95	0.73	0.96
Hospital admissions				
Hospital admission (%)	5.5	9.4	7.3	11.7
Hospital admission per patient per year	0.09	0.16	0.10	0.16
Hospital days per patient per year	0.6	1.2	1.42	2.13
Adverse events				
All discontinuations (%)	18.7	27.8	15.2	21.2
Adverse event discontinuations (%)	9.6	13.7	10.1	12.8
Lack of efficacy discontinuations (%)	2.4	7.0	0.8	1.7

238/550 (43%) with control. The NNT to prevent one patient having at least one exacerbation in a year was 13 (95% CI 8-41). At least one hospital admission occurred in 56/906 (6%) of patients treated with tiotropium compared with 56/550 (10%) with control. The NNT to prevent one patient having at least one admission in a year was 25 (14-97).

Only about 10% of patients had a hospital admission with the control treatments, but the average number of hospital days for each patient was 1-2. That means that when a patient with COPD has a hospital admission it is for at least 10 days. Tiotropium saved at least 0.6 of a hospital day a year for each patient given tiotropium. The most common adverse event with tiotropium was dry mouth. All discontinuations, and adverse event discontinuations, were lower with tiotropium than with control.

Comment

These results hang together. There is good evidence that FEV1 is an important clinical measure, and predicts exacerbation and hospital admission for patients with COPD in primary care, as well as mortality when admitted. Improvement in FEV1 should logically then result in lower rates of exacerbation and hospital admission. This they do with tiotropium in large, high quality, long-duration trials.

So what we have is good evidence for clinical efficacy of tiotropium at various levels, from respiratory physiology to important healthcare outcomes. The question then is how important are these results for healthcare services and delivery.

Health economics and perspective

The first place to go for sensible thoughts about COPD is the British Thoracic Society guidelines [8]. As well as having useful thoughts on management of the disorder, it also tells us much about the impact of COPD on emergency services. For instance, about 12% of all medical emergency admissions in the UK are due to COPD (or were in the early '90s). Using some of the figures for annual GP consultations with COPD, we can conclude that an average primary care organisation (PCO) of 100,000 people would have about 2,600 consultations for COPD (Table 2). That's half to one GP, though other estimates for GP consultations are much higher, at about three per patient per year [9].

Table 2: COPD consultations in a PCO

Age	Number	Rates per 10,000	COPD consultations per PCO
45-64	19000	417	792
65-74	12000	886	1063
>75	7000	1032	722
Total	38000		2578

An estimate of the burden of COPD in the UK based on data from the early '90s indicated the cost to the NHS of managing COPD was over £800 million [9]. A detailed breakdown of those costs is in Table 3. The estimate is likely to be out of date, since emergency admissions for COPD have risen by 50% since the mid-90s, to about 100,000 a year in 2000. That's about 200 emergency admissions for COPD for each PCO, at a cost of about £3000 [9], or about £600,000 per PCO.

Table 3: Estimated costs of COPD care in the UK in the early 1990s

Item	Cost (£ million)
Inpatient stay	243
GP consultations	237
Outpatient clinic	35
Prescribing	126
Diagnostic tests	144
Other	20
Total	805

Another critical issue is the consumption of bed-days in hospital. An early UK estimate is that COPD patients consumed 1.2 million bed days a year in the early 1990s. Table 4 shows that estimate to more or less agree with the results of the tiotropium clinical trials, with some back of envelope assumptions about prevalence of COPD and the proportion of COPD patients who have moderate or severe disease. It suggests that translating the results to a UK perspective could save the equivalent of 528,000 bed days, the equivalent of four 400 bed hospitals. Whether the intervention is cost effective would depend on a thorough cost-effectiveness analysis, and that includes the crucially important issue of acquisition cost, something we don't yet have as this intervention is not yet licensed.

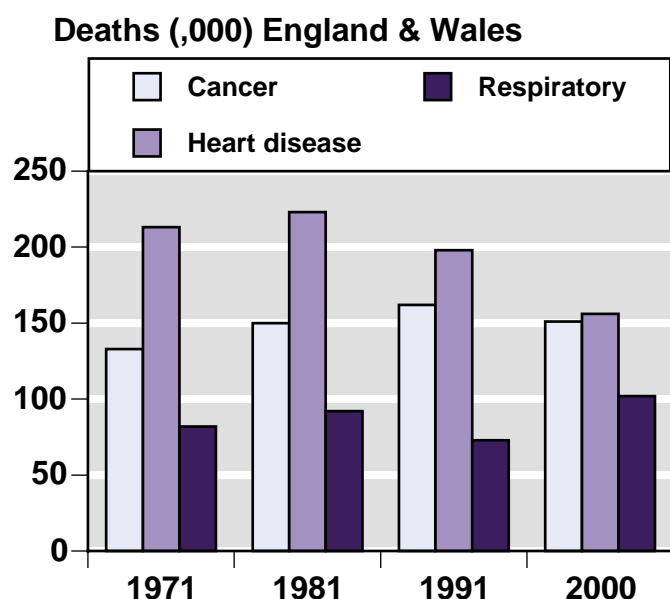
Table 4: Some preliminary health economic calculations for COPD admissions in the UK

Item	Assumption	Per 100,000	Per million	Per 55 million
Number of patients with COPD	10% prevalence in over 40s	4,000	40,000	2,200,000
Moderate or severe COPD, FEV1 <70% predicted	Assume 40% of all COPD	1,600	16,000	880,000
Number of hospital days	1.7 days per patient per year, mean of US and European	2,720	27,200	1,496,000
Number of bed days saved with tiotropium	Average saving 0.6 days per patient per year	960	9,600	528,000
Cost saving (£) possible on hospital admission	Assume £200 per day	192,000	1,920,000	105,600,000

These simple calculations take no account of how new technology can impact on the perennial problem of health service capacity. When beds, doctors and nurses are at a premium because we don't have enough, we should value interventions like this more highly.

One thing we do know, and that is deaths from respiratory diseases are rising (Figure 1). COPD will be a bigger problem with population ageing. More and better health economic studies will enable us to plan services better.

Figure 1: Death rates in England and Wales



References:

- 1 DC McCrory et al. Management of acute exacerbations of COPD. *Chest* 2001 119: 1190-1209.
- 2 PB Bach et al. Management of acute exacerbations of chronic obstructive pulmonary disease: a summary and appraisal of published literature. *Annals of Internal Medicine* 2001 134: 600-620.
- 3 M Miravittles et al. Factors associated with increased risk of exacerbation and hospital admission in a cohort of ambulatory COPD patients: a multiple logistic regression analysis. *Respiration* 2000 67: 495-501.
- 4 J Vestbo et al. Vital prognosis after hospitalisation for COPD: a study of a random population sample. *Respiratory Medicine* 1998 92: 772-776.
- 5 R Casaburi et al. A long-term evaluation of once daily inhaled tiotropium in chronic obstructive pulmonary disease. *Eur Respir J* 2002 19: 217-224.
- 6 V Vincken et al. Improved health outcomes in patients with COPD during 1 yr's treatment with tiotropium. *Eur Respir J* 2002 19: 209-217.
- 7 PJ Rees. Tiotropium in the management of chronic obstructive pulmonary disease. *Eur Respir J* 2002 19: 205-206.
- 8 Anon. BTS guidelines for the management of chronic obstructive pulmonary disease. *Thorax* 1997 52: Suppl 5.
- 9 JF Guest. The annual cost of chronic obstructive pulmonary disease to the UK's National Health Service. *Dis Manage Health Outcomes* 1999 5: 93-100.

Bandolier 92 reported a meta-analysis of trials looking at a comparison of stents versus balloon angioplasty indicating stents to be better. With stents the death rate was 3.8% and reinfarction rate 2.1% over six months in randomised trials up to 1999. The interesting question is whether this retrospective analysis represents what is happening in today's clinical practice, with technical advances and improved anticoagulation. An analysis of ongoing studies suggests that death and reinfarction rates are lower now than they were [1].

Study

Six major clinical trials of coronary stenting were coordinated from Boston, all using similar inclusion criteria and protocols, but with different stents. Protocols used routine high-pressure postdilation, and with aspirin 325 mg daily and ticlopidine 250 mg twice daily for four weeks, but with glycoprotein IIb/IIIa inhibitors discouraged.

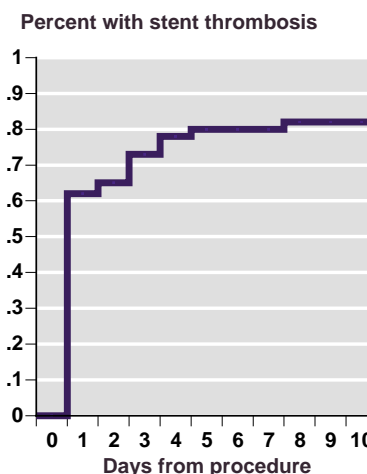
All used stent thrombosis as a clinical endpoint, and with the same definition of clinical and angiographic stent thrombosis and myocardial infarction. From the paper it appears that some, but not all, of the trials were randomised.

Results

In all there were 6,186 patients who received a stent. Thrombosis occurred in 53 of them (0.9%), and thrombosis was confirmed angiographically in 45 of the 53. Most stent thromboses occurred within the first two days after the procedure (Figure 1), and events after one week were rare. With thrombosis mortality was 19% at one month and 21% at six months. Mortality or myocardial infarction with thrombosis was 70% at one or six months. Overall mortality was 10 in 6,186 (0.2%) at one month.

Predictors for clinical stent thrombosis were persistent dissection after stenting, longer stent length and final minimal lumen diameter. Unstable angina, use of glycoprotein IIb/IIIa inhibitors, nonrandomised versus randomised status nor stent type were not associated with any significant stent thrombosis.

Figure 1: Thrombosis after stenting



Bandolier occasionally sees surgeons getting a bashing for not being “evidence-based” about their work. While that may occasionally be true, there are lots of systematic reviews for surgery and the perioperative period, and lots of randomised trials. But the challenges are different and sometimes different approaches are needed.

Here we see the benefits of a registry of ongoing trials, some randomised, some not, but all benefiting from common outcomes and design that allows mature overview. In industrial manufacture this would be called quality control,

a sort of high-level “kaizen” working to continually improve quality and competitiveness.

The bottom line for the moment is that the prognosis with stent thrombosis is dire. But we know when it occurs, and we know some of the predictors, so that although it is uncommon, that already low rate can be reduced even further.

References:

- 1 DE Cutlip et al. Stent thrombosis in the modern era. A pooled analysis of multicentre coronary stent clinical trials. *Circulation* 2001 103: 1967-1971.

CABG MORTALITY

A reader asked the question about what were the death rates after coronary artery bypass grafting (CABG) and whether there were any patient criteria that predicted a higher likelihood of dying. Good questions these, and there is some quite interesting evidence to look at.

CABG mortality by sex and age

In the United States the National Cardiovascular Network collects information on patient characteristics, post CABG complications and (short-term) in-hospital mortality, using trained personnel from a number of hospitals. Between October 1993 and December 1999 there were complete data on just over 51,000 CABG patients; 30% were women. Mortality and major post surgery complications were examined by age and sex, together with interactions with pre-existing patient characteristics, like comorbid conditions.

Crude mortality rates by age and sex are shown in Figure 1. Women had higher death rates than men, an effect apparent until the ninth decade of life. Women, and younger women in particular, were more likely to have other conditions like diabetes, heart failure, stroke and hypertension. Making allowances for these reduced the difference between men and women, but did not eliminate it.

Women also tended to suffer more postoperative complications than men (Table 1), except for bleeding requiring

Table 1: Post CABG complications

Complication	Percentage with complication	
	Men (36,009)	Women (15,178)
Bleeding requiring reoperation	3.0	2.9
Postoperative MI	1.3	1.7
Neurological complication	3.8	5.3
Renal failure	4.0	5.0

reoperation. Again, the difference between women and men was most marked at younger age.

The cause of the higher mortality and complication rates in younger women is not known. While younger women are more ill, this does not account for all the difference, and an unknown risk factor has been postulated.

BMI and CABG mortality

In the United States a randomised trial of CABG and percutaneous transluminal coronary angioplasty (PCTA) has been going on, and patients declining randomisation have been entered into a concurrent observational registry. Patients have been followed up for five years. Short and long-term outcomes have been analysed according to initial BMI for all CABG patients [2].

Examination of the 1,503 patients undergoing CABG according to BMI showed no effect of BMI on in-hospital events. Three and five-year (Figure 2) mortality after CABG was very significantly affected by BMI. The reason for the link between BMI and mortality is likely to be an increased presence of multiple coronary risk factors in obese patients.

Which CABG procedure

Most people undergoing CABG need three bypass grafts, with a single internal mammary artery graft and two vein grafts. The evidence for the use of arterial graft is good, but what about the evidence for using two internal mammary grafts instead of one? A thoughtful meta-analysis indicates that two is likely to be better than one [3].

The review sought studies comparing single and bilateral

Figure 1: In-hospital CABG mortality

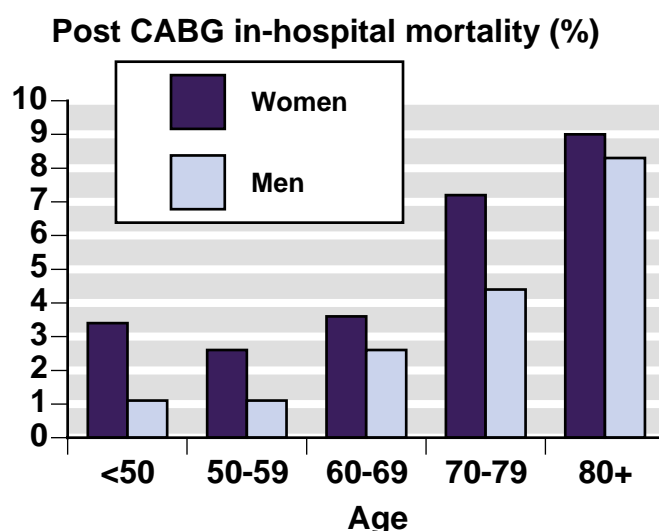
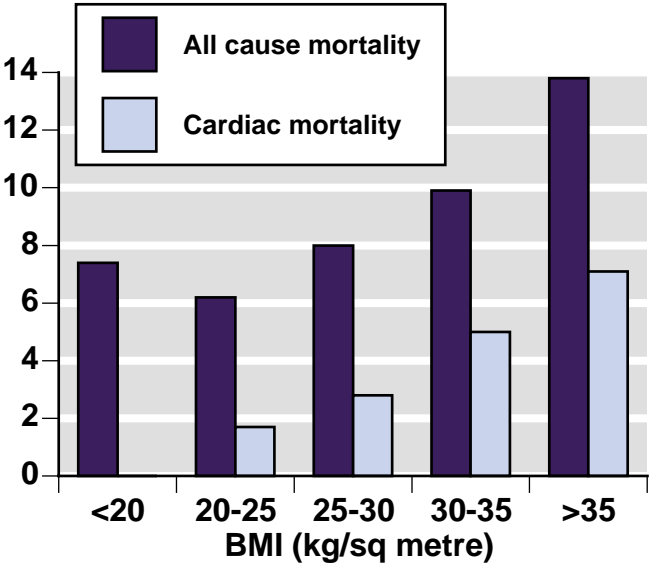


Figure 2: Five year mortality and BMI

Percent five year mortality



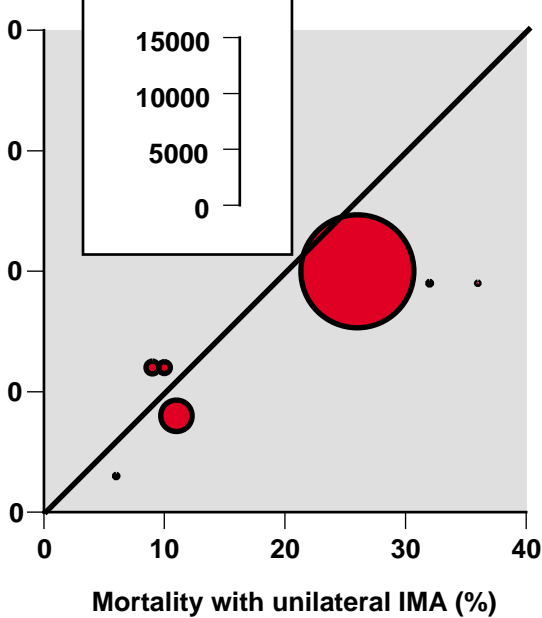
internal mammary grafts that had at least 100 patients in each group and with at least four years of follow up. Study quality was assessed on a variety of criteria. Particularly interesting was the quality assessment of non-randomised studies (Table 2) that included comparability at baseline.

There were 10 reports included, and seven had information that could be combined. None of the reports was a randomised trial, but most scored highly in the quality assessment exercise. The bulk of the patients (81%) and deaths (87%) were in two large studies.

The seven studies had 15,962 patients, and there were 679/4693 (14%) deaths at longest follow up with bilateral interior mammary artery grafts, and 2482/11269 (22%) for single mammary artery grafts. This was statistically significant, with a hazard ratio of 0.80 (0.70 to 0.94). If one were to calculate an NNT for bilateral versus single internal mammary artery grafts to prevent one long-term death it would be 13 (11-16). Redo surgery rates were also lower with bilateral grafts (8% versus 40% in the largest trial).

Figure 3: Single and bilateral IMA grafts

Mortality with bilateral IMA (%)



Comment

There is a fascinating wealth of evidence of different types available in the field of surgery, including many systematic reviews and meta-analyses of randomised trials, together with large comprehensive registries, and much thoughtful stuff besides. For CABG even a cursory examination of evidence tells us much about likely short- and long-term survival. But we have also to remember that in 1958 randomised trials told us that internal mammary artery ligation for angina was ineffective. So randomisation is not to be overlooked! Caveat lector.

References:

- 1 V Vaccarino et al. Sex differences in hospital mortality after coronary artery bypass surgery. Evidence for higher mortality in young women. *Circulation* 2002 105: 1176-1181.
- 2 HS Gurm et al. The impact of body mass index on short- and long-term outcomes in patients undergoing coronary revascularization. *Journal of the American Collage of Cardiology* 2002 39: 834-840.
- 3 DP Taggart et al. Effect of arterial revascularisation on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. *Lancet* 2001 358: 870-875.

Table 2: Quality assessment of non-randomised studies

Cohort selection was assessed on the answers to three questions	
Were details of criteria for assignment of patients to treatment provided?	One star awarded for relevant details.
How representative was the exposed cohort?	One star if representative of typical patient, no star if groups of patients were selected or selection of group was not described.
How was the non-exposed cohort selected?	One star if drawn from the same community as the exposed cohort; no star if drawn from a different source, or selection of group not described.
Cohort comparability was assessed on the basis of study design or analysis of cohort differences	
No differences between the two groups, or differences controlled for, in particular with reference to age, sex, and relevant clinical status (two stars). One star was assigned if one of these characteristics was not reported, even if there were no other differences between the groups, and the other characteristics had been controlled for. No star was assigned if the two groups differed.	
Outcome was assessed by two criteria	
Assessment of outcome	One star for information ascertained by record linkage or interview, no star if this information was not reported or ascertained in some other way.
Adequacy of cohort follow-up	One star if no patient or fewer than 20% of patients were lost to follow-up; no star if more than 20% of patients were lost to follow-up, or if the researchers did not provide relevant information.

Do FORMULARIES WORK?

Formularies for medicines are used for quality control of care (antibiotics, parenteral feeding) and to reduce prescribing costs. There will always be good reasons why some pharmaceutical products should not be available, but what is the evidence that broader restrictions on availability have any effect on cost or care quality? Prompted by evidence from a randomised trial that patients switched antidepressants frequently (*Bandolier* 95), a reader asked what evidence was there that formularies reduced cost, improved care, or both?

All other considerations being equal, an initial choice based on prescription costs is prudent, ethical, and clinically reasonable. Benefits at least in cost should follow this as night follows day. *Bandolier* expected a large literature and some good literature reviews. We found neither.

Search

PubMed was searched using the terms formulary and pharmacy together or separately, using limits of meta-analysis, review, and randomised controlled trial. Review articles and textbooks were also examined for relevant references. The aim was (in order) to find systematic reviews, reviews, or randomised trials looking at broader formulary restriction. When this strategy produced almost nothing of relevance, the search was repeated with prescribing and restriction.

Trial

One randomised trial [1] was found, that randomised physicians to prescribing a limited set of dosages of thyroxine. Thirty-three physicians prescribing thyroxine were randomised (open-label) by a computer to one of two formu-

lary systems. One restricted thyroxine doses to 25, 50, 100, 125 and 150 µg, while the other had more dose strengths available (25, 50, 75, 100, 112, 125, 150, 175, 200, and 300 µg). Treatment efficacy was assessed by examination of thyroid function test results of patients prescribed thyroxine under the two systems, in patients taking thyroxine and newly prescribed for more than three months. Prescriptions were also analysed, and their cost calculated.

Results

Physicians in the restricted group were four years older than average, but otherwise there was no difference between the physicians in terms of clinical experience. There were 241 eligible patients. Thyroid function test results were the same (on average) for patients with similar conditions. Average doses prescribed were the same. Clinic visits were identical. Dose changes were the same. Prescriptions filled were the same. Cost was the same. Tablets prescribed were different (Figure 1).

Comment

This was a successful experiment, in that it demonstrated that simplifying the doses of thyroxine available to prescribing physicians did not adversely affect patients, or increase costs. But then, 10 dose strengths for thyroxine seemed a bit excessive: MIMS has three.

This was a good trial which was conducted at the National Institutes of Health and various major sites in the USA. The trouble is that it does not prove that formulary restriction on a wider basis reduces costs or improves health outcomes. Indeed, what little *Bandolier* could find suggested the opposite.

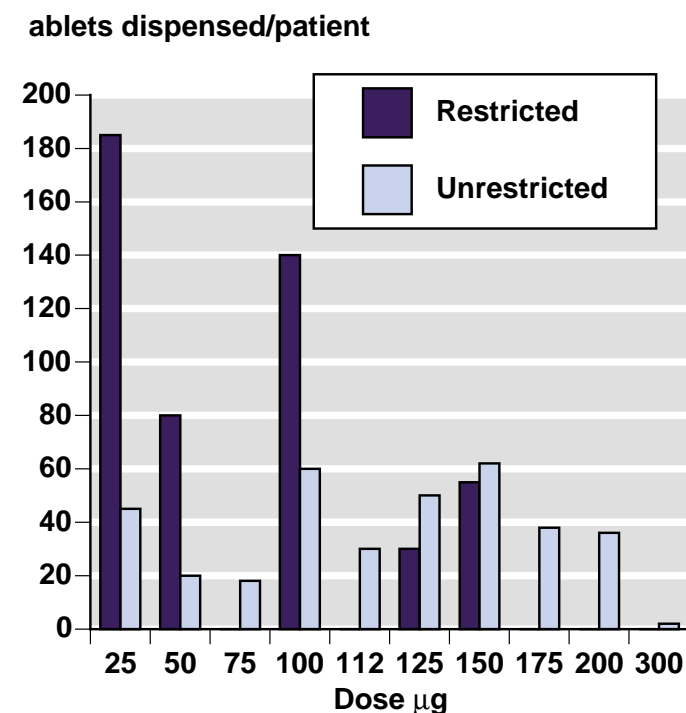
One study [2] study provided empirical evidence of the influence of hospital formulary restrictions on pharmacy charges, all other hospital charges, and on length of stay, using a survey of hospital drug policies and hospital discharge data from Washington State in 1989. Some drug costs increased, others decreased, and some stayed the same. Across-the-board restrictions did not result in cost savings, although savings may be realized for particular drug categories. And a very recent review of using pharmacoeconomic influences [3] concluded that acquisition cost was the prime influence on formulary decisions, rather than overall healthcare costs and quality.

Where's the beef? Perhaps *Bandolier* has missed a huge literature of real importance. We'd love pharmacists and others who know this evidence to tell us where to find it, so that we can reprise this topic in a future issue.

References:

- 1 KB Ain et al. Effects of restricting levothyroxine dosage strength availability. *Pharmacotherapy* 1996 16: 1103-1110.
- 2 FA Sloan et al. Hospital drug formularies and use of hospital services. *Med Care* 1993 31 :851-67.
- 3 DC Suh et al. Application of pharmacoeconomics to formulary decision making in managed care organizations. *Am J Manag Care* 2002 8:161-9.

Figure 1: Tablets dispensed per patient for each of thyroxine dosage form available



BANDOLIER SUBSCRIPTION FORM

Important

**All existing non-subscription distribution will end in July 2002 and from August 2002 Bando-
lier will be available only by subscription direct from us. If you wish to continue to re-
ceive Bando-lier after July you have to complete this form and return it to us in good time.**

Title you want us to use

Name

Address

Address

Address

Postcode and country

Email

Phone or fax

Tel

Fax**Invoice address if different**

I would like to subscribe for 12 issues

UK & N Ireland £36 ☐Rest of the world £72 ☐**Payment options (Pounds Sterling only) including postage**

Cheque (UK only) ☐

International Money Order (RoW & Ireland)

Please make cheques payable to Bandolier

Visa

☐

Mastercard



7

Name on card**Card number****Expiry date**

Signature

Date

Please send the completed form by fax to

+44 (0)1865 226978, or with payment, to:

**Maura Moore
Bandolier Subscriptions
Pain Research
The Churchill
Oxford OX3 7LJ, UK**

**Bandolier would be delighted to quote for bulk orders to organisations, especially healthcare institutions or charities, or for bulk reprints, all at preferential rates:
Email: maura.moore@pru.ox.ac.uk**